Remarks

Amendment to Specification

Applicants have amended paragraphs 0015 and 0020 to insert the term "daltons" as the unit of molecular weight for the proteins discussed in those paragraphs. These paragraphs are amended to provide support of the amendments to Claim 1-5 and 13-14 discussed below. Applicants respectfully submit that persons of skill in the art would be familiar with the term dalton as a unit of measurement and its proper application to glycoproteins having the weight range disclosed in the instant application as originally filed.

The §112, second paragraph Rejections of Claims 1-37

The Examiner rejected Claims 1-5 and 13-14 under 35 U.S.C. § 112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention. Specifically, the Examiner states that Claims 1-5 and 13-14 are indefinite for not stating whether the units of molecular weight are daltons or kilodaltons. Applicants thank the Examiner for pointing out this omission.

Applicants have amended Claims 1-5 and 13-14 to include the term "daltons." Applicants respectively submit that this unit of measurement would be clear to those having skill in the art. Applicants respectfully request removal of the rejections of Claims 1-5 and 13-14 under §112, second paragraph.

The Examiner rejected Claims 25, 35, and 37 as indefinite and confusing citing the lack of a definition of functional food product in the specification. Claims 25, 35, and 37 have been amended by deleting the term "functional" thereby removing the undefined term from the rejected claims. Applicants respectfully request removal of this rejection of Claims 25, 35, and 37 under 35 U.S.C. §112, second paragraph.

Finally, the Examiner rejected Claim 25 as indefinite and vague for claiming a health food or food product which may claim antidiabetic, antihypertensive, antiobesity, and antihyperlipidemic activities. Applicants have amended Claim 25 to claim a health food or food

product which claims "at least one" of the antidiabetic, antihypertensive, antiobesity, and antihyperlipidemic activities. Support for this amendment can be found in paragraphs 0031-0033 of the specification describing the incorporation of the claimed glycoprotein in health food and food products and also through the Detailed Description of the invention describing tests demonstrating the antidiabetic, antihypertensive, antiobesity, and antihyperlipidemic activities of the glycoprotein. Applicants respectfully request removal of this rejection of Claim 25 under 35 U.S.C. §112, second paragraph.

The §102 (b) Rejections of Claims 1, 3, 4, 6, 9, 10, and 12

The Examiner rejected Claims 1, 3, 4, 6, 9, 10, and 12 under 35 U.S.C. §102 (b) as anticipated by U.S. Patent No. 5,854,404 to Nanba, et al. ("Nanba" or "the Nanba patent"). Applicants have amended Claim 1 from which Claims 3, 4, 6, 9, 10, and 12 directly or indirectly depend. Applicants respectfully traverse the rejection of Claims 1, 3, 4, 6, 9, 10, and 12 as amended and request reconsideration.

"A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described in a single prior art reference." *Vandergaal Bros. v. Union Oil of California*, 814 F.2d 628, 631; 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). MPEP § 2131. (Emphasis added.) Applicants respectfully submit that the Nanba patent fails to disclose all the elements of independent Claim 1 as amended and thus fails to anticipate that claim. First, Applicants have amended Claim 1 to claim the performance of each of the steps of the claimed method in order meaning the order listed in Claim 1. Specifically, in the claimed method, the first step is the extraction of the *Grifola* fruiting body with ethanol at room temperature followed by the extraction of the residue with hot water. In contrast, Nanba only discloses an extraction process in which the first step is the extraction of the Grifola fruiting bodies with water followed by a second extraction of the step in which ethanol is added to the water soluble fraction produced by the initial water extraction. As is well known in the art, the order in which extraction steps are performed can result in the extraction of different products. Moreover, the

Nanba patent makes no explicit disclosure of the step of initially extracting the *Grifola* fruiting bodies with ethanol.

Moreover, Applicants' respectfully submit that the claimed method results in a different product than the product disclosed in the Nanba process. Applicants first point out that in the preamble of Claim 1, the method that is claimed is a method for preparing a bioactive glycoprotein. In fact, Claims 13 and 14 both claim the glycoprotein having a protein to saccharide ratio ranging from 75:25 to 90:10. Applicants respectfully submit that glycoproteins are defined as conjugated proteins whose conjugates are carbohydrates in which the carbohydrate is either a monosaccharide or a short oligosaccharide. (See *Dictionary of Biochemistry and Molecular Biology, 2d Edition*, J. Stenesh, John Wiley & Sons, NY. p. 201) In contrast, the Nanba patent discloses that the substance formed is a "glucan/protein complex where the glucan/protein ratio varies mainly in the range of 80:20 to 99:1..." After purification by column chromatography, the substance in Nanba was found to have a glucan/protein ration of 96:4. (See Nanba, col. 3, lines 6-8). Compounds of this type are defined as proteoglucans. *Ibid*, p. 388. Consequently, it can be seen that Applicants claimed method results in the extraction of a completely different type of product in which the glucan/protein ration is 25:75 to 10:90 (protein heavy) which is the reverse of the glucan:protein ratio in the product disclosed in the Nanba patent (carbohydrate heavy).

Therefore, Applicants respectfully submit that the Nanba patent fails as a reference under §102 (b) as it fails to disclose all the elements of amended Claim 1. Specifically, the Nanba patent fails to disclose the initial extraction of *Grifola* fruiting bodies with ethanol followed by a second step of extraction with hot water. In addition, the steps disclosed in the Nanba patent result in a different product than the product produced by Applicants claimed method. Therefore, the Nanba patent fails to disclose each element of amended Claim 1 as set forth in that claim. Applicants respectfully request reconsideration and allowance of Claim 1.

Claims 3, 4, 6, 9, 10, and 12 depend from Claim 1 and thus incorporate all the limitations of that claim. Because, as discussed above, the Nanba patent fails to anticipate all the elements

of Claim 1, it also fails to anticipate Claims 3, 4, 6, 9, 10, and 12. Applicants respectfully request the removal of the rejections of Claims 3, 4, 6, 9, 10, and 12 and allowance of those claims.

The §103 (a) Rejections of Claims 1-37

The Examiner rejected Claim 1-37 under 35 U.S.C. §103 (a) as obvious over the Nanba patent in view of Kubo, et al. in *Biol. Pharm. Bull.*, vol. 17, No. 8, pp 1106-1110, 1994 ("Kubo" or "the Kubo reference"). Applicants respectfully traverse these rejections and request reconsideration.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. In addition, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The Examiner cites the Nanba patent as disclosing the method claimed in Claims 1-12 and the Kubo reference as disclosing the use of the bioactive glycoprotein claimed in Claims 13 and 14 in food products and as an antidiabetic, antihypertensive, antihyperlipidemic, and/or antiobesity compound as claimed in Claims 15-37. First, Applicants respectfully traverse the Examiner's statement that the Nanba patent "clearly discloses a method for preparing a bioactive glycoprotein." As noted above, Nanba discloses the extraction of a completely different compound than claimed in Claims 13 and 14 and also discloses a different extraction method (an initial water extraction rather than an initial ethanol extraction). In fact, the compound disclosed and characterized by the Nanba patent is not a glycoprotein at all but a proteoglucan with a glucan:protein ratio completely reversed from the ratio of the glycoprotein claimed by Applicants Therefore, there is no teaching or suggestion in the Nanba patent of the actual glycoprotein claimed by

Applicants' Claims 13 and 14 nor does Nanba speculate or discuss any extraction methods other than the initial water extraction method disclosed in the Nanba patent.

Regarding the Kubo reference, the Examiner only cites it to demonstrate the use of maitake as a source of an antidiabetic, antihypertensive, antihyperlipidemic, and/or antiobesity compound as claimed in Claims 15-37. Again, Applicants respectfully traverse the Examiner's statement that the Kubo reference provides sufficient clarity and motivation to one of ordinary skill in the art to combine with the Nanba patent to render Applicants' claimed method and compound obvious. Like Nanba, Kubo makes no suggestion or teaching that Applicants' claimed glycoprotein product acts as an antidiabetic, antihypertensive, antihyperlipidemic, and/or antiobesity compound. Also, again like Nanba, Kubo only discloses proteoglucans with a higher proportion of carbohydrate than protein, as opposed to Applicants protein heavy glycoproteins. In fact, Kubo actually teaches away from the use or desirability of Applicants' claimed method to extract Applicants' claimed glycoprotein. Applicants acknowledge the Examiner's statement pointing specifically to the ES and X fractions in *Basidiomycetes* that are shown in Kubo to have antidiabetic activity, and his remarks that that the other fractions were found to be inactive. In point of fact, the Examiner's statement points out why Kubo teaches away from Applicants' invention. Figure 4 in Kubo depicts the effect of various maitake (*Grifola*) fractions on blood glucose levels in diabetic rats. Graph b of Figure 4 shows the effects of the YS fraction which is the same fraction that is the source of Applicants' claimed glycoprotein. As seen in Graph b, the increase in blood glucose after treatment with YS fraction is virtually identical with that of control (untreated) mice shown in Graph a with both graphs showing no antidiabetic activity. Therefore, these results teach away from both Applicants' invention of the method of Claim 1 to extract and separate the bioactive glycoprotein claimed in Claims 13 and 14 <u>from the YS fraction</u> and the actual glycoprotein claimed in Claims 13 and 14. Therefore, Kubo provides no motivation to a person of ordinary skill in the art to extract a glycoprotein <u>or any other type of compound</u> from the YS fraction to find an antidiabetic compound as Kubo teaches the YS fraction as having no antidiabetic effect at all. Applicants also respectfully point out that Kubo

fails to show or discuss any other type of bioactivity of the YS fraction. Consequently, Kubo fails to provide any motivation to a person of ordinary skill to further fractionate, filter, or otherwise separate the components of the YS fraction to find desirable bioactive compounds in that fraction because, as noted by the Examiner, Kubo teaches that the YS fraction is inactive.

For a second, similar reason, the combined Nanba and Kubo references fail to render the method of Claim 1 obvious as they fail to teach or suggest all the elements of either independent Claim 1 directed to the method of extraction or independent Claims 13 and 14 directed to a glycoprotein of 14,000 daltons or 20,000 daltons, respectively. Specifically, neither Nanba nor Kubo teaches or suggests the collection of the fraction of molecular weight equal to 14,000 from the resulting supernatant. As noted above, the method disclosed in Nanba does not result in the same fraction as it starts with a different first step. Second, Kubo does not disclose fractionation or any type of collection or refinement of the analogous YS fraction and as noted above, provides no motivation to a person of ordinary skill in the art to proceed with the claimed collection step. Therefore, for this second reason, specifically a lack of teaching or suggestion of all the elements of Claims 1, 13 and 14, the combined Nanba and Kubo references fail to establish a *prima facie* case of obviousness to render Claims 1, 13, and 14 obvious. Applicants respectfully request reconsideration and allowance of Claims 1, 13, and 14.

"If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious." *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Claims 2-12 depend from Claim 1 and thus incorporate all the limitations of that claim. Because, as discussed above, the Nanba patent and Kubo reference fail to render obvious Claim 1, they also fails to render obvious Claims 2-12 Applicants respectfully request the removal of the rejections of Claims 2-12 and allowance of those claims.

Similarly, Claims 15-37 depend from either Claim 13 or 14 and thus incorporate all the limitations of those claims. Because, as discussed above, the Nanba patent and Kubo reference fail to render obvious Claims 13 and 14, they also fail to render obvious Claims 15-37.

Applicants respectfully request the removal of the rejections of Claims 15-37 and allowance of those claims.

Conclusion

Applicants respectfully submit that the present application is now in condition for allowance, which action is courteously requested. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully yours,

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